Use of Complementary and Alternative Therapies in Children

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The use of complementary and alternative therapies in children has recently shown explosive growth, despite little scientific evidence of benefit, a need for better regulatory oversight, and continuing gaps in the knowledge and attitudes of pediatric health professionals.

Epidemiology

A dietary supplement is defined by the National Center for Complementary and Alternative Medicine (NCCAM) as a product (other than tobacco) that is intended for use by humans to supplement the diet by increasing total dietary intake and that bears or contains one or more of the following ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, or a dietary substance.[1] Dietary supplements are in the marketplace in unprecedented numbers, and consumers are likely to spend increasing amounts on these products in the future. Whereas there were about 4,000 supplements on the US market in 1994, the General Accountability Office has estimated that upward of 75,000 such products were available in 2008 and reported that US sales of dietary supplements reached $27.7 billion in 2007, with half of all Americans reporting use of these products.[2]

In one study, as many as 70% of parents said they give their children herbs and dietary supplements to preserve their good health as well as to treat minor illnesses.[3] Special populations, including immigrants and ethnic minorities, often give traditional remedies containing herbal ingredients to their children. Unfortunately, many such remedies, including unregulated, imported products, may be of poor quality or may contain undeclared drugs, chemicals, metals, or other adulterants or contaminants, which can cause serious poisoning in children. Use of dietary supplements continues its high prevalence in adolescence. Products that claim to enhance sports performance or promote energy or weight loss are especially popular. It seems reasonable, therefore, to ask whether health-care providers for infants, children, and adolescents up to age 21 years should or should not endorse the use of herbs and dietary supplements in children, let alone provide guidance to parents concerning the advisability and safety of specific products.

Current policies

Parents assume that herbs and many dietary supplements are "natural" and therefore safe and effective. They also assume that they are regulated in the same way that prescription medications are by the US Food and Drug Administration (FDA). Both are false assumptions. Parents most frequently cite their children's health-care provider as a primary source of reliable information on all matters concerning their children's health, including the advisability of dietary supplement use. Yet they often treat their children's ailments with home remedies, herbal therapies, or over-the-counter products without any input from health professionals and do not discuss use of herbs and dietary supplements with their children's doctors.[3]

Furthermore, health professionals are largely uninformed about the evidence-based medical uses of such products and their safety. Although the majority of schools for health professionals now offer some coursework in complementary and alternative medicine, the educational content does not necessarily provide detailed information about herbs and dietary supplements, address cultural competency in communicating with parents about their use of supplements, give instructions on how to report adverse effects to the FDA, or teach how to document such use routinely in the medical record.

Health-care institutions give evidence of ambiguous policies when it comes to herbs and dietary supplements. The results of our recent survey of 109 US children's hospitals indicated that only 2% of hospital formularies included herbs and only 38% included other dietary supplements.[4] Still, 84% of the same children's hospitals surveyed would allow a hospitalized child to use a home supply of dietary supplements. This suggests an ambivalent approach to the therapeutic value of such products. Allopathic health professionals do not want to be the purveyors of herbs and supplements, but they acknowledge and support their use by the lay public, often without much informed input into parental decision making with respect to the potential risks and benefits.

Benefits vs. danger

As parents look for environmentally safe, nonpharmaceutical remedies for their children, the marketing of products intended for children has expanded, and there is a danger in parents being misled by unsubstantiated marketing claims. Unfortunately, there are few clinical studies supporting the use of herbs and dietary supplements for the treatment of common childhood conditions. Although more pediatric studies are planned, there are many research and ethical barriers to building this evidence base, thus leading to a dearth of randomized controlled trials to give credence to claims of herbal and dietary supplement efficacy for children. Such proof of efficacy and safety is especially needed in infants and young children, whose small size, sensitive and developing organs, and immature immune and detoxification systems make them more vulnerable than adults

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to allergic reactions and adverse effects from a chemical or xenobiotic in a plant or supplement. More research is also needed into additive risks from mixtures of dietary supplements or their interactions with drugs when both are taken together by children. Moreover, the usefulness of such products must be weighed against the known clinical value and risk of more conventional therapies.

The National Institutes of Health (NIH) has incurred tremendous expenditures on research investigating the medical value of complementary and alternative medicine, but relatively few studies have been completed in children. The NCCAM (part of the NIH) has spent more than $1 billion on research from fiscal year 1999 to 2009 (see **Figure 1**), but as yet its website provides no functionality for informing the public as to which specific dietary supplements have been proven safe and effective for use in children.[1] The NCCAM laments the continuing lack of rigorous scientific studies investigating the use and safety of dietary supplements in children. In fiscal year 2008, the NIH spent $298 million on complementary and alternative medicine research, but only $1.4 million (or less than 0.5% of the total) was expended by the National Institute of Child Health and Human Development.[5] Thus, there is evidence of a lack of commitment to investigating both the efficacy and the safety of dietary supplements in children, even though an uncontrolled experiment is going on daily via the easy accessibility and widespread uninformed use of such products.

There is a "buyer beware" mentality regarding the contents and quality of many dietary supplements. Some products still bear claims of health benefits that are not scientifically proven in children. Other problems include undeclared ingredients, inadequate warnings, a lack of child-resistant packaging, and absent pediatric dosing guidance.

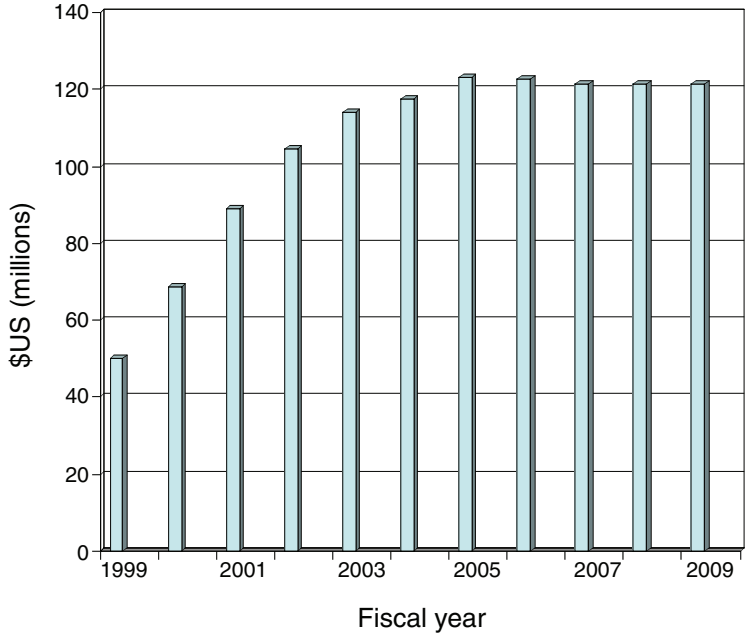

Figure 1 National Center for Complementary and Alternative Medicine funding, fiscal years 1999–2009. From ref. 5.

Measured approach

In 2005, the American Society for Clinical Pharmacology and Therapeutics (ASCPT) published a position statement on herbs and dietary supplements that contained important recommendations.[6] Some of these, such as the inclusion of manufacturers' telephone numbers on labels and the mandating of manufacturer reporting to the FDA of serious adverse events involving its products, have come to fruition. In 2008, in accordance with another ASCPT recommendation, the FDA released a new good manufacturing practices regulatory guidance, which should improve the quality of domestically produced dietary supplements.

Yet the ASCPT white paper did not specifically address the needs of children and adolescents. Children rely on adults to make informed decisions regarding their health and well-being, and parents and other caregivers have a duty to seek out the best treatments for them. We endorse the ASCPT recommendations but believe that there are six critically important initiatives necessary to safeguard the interests of children:

1. Congress should empower the FDA with needed expanded regulatory oversight and funding so as to monitor adequately the manufacture, labeling, safety, health benefits claims, and postmarketing testing and monitoring of herbs and dietary supplements intended for children.
2. Health professionals both in training and in clinical practice should inform themselves broadly regarding the safety and effectiveness of herbs and dietary supplements before giving advice to families or recommending specific products for use in pediatric patients. They also should be educated in the recognition and reporting of adverse effects from such products. Additionally, governmental agencies should issue appropriate guidance specific to the use of dietary supplements by children and adolescents to the public and health professionals alike.
3. Governmental agencies should assign a higher priority than is currently evident to the scientific study of herbs and dietary supplements in the context of their efficacy and safety for use by children and adolescents.
4. As a corollary to the above recommendation, new and existing pediatric clinical pharmacology units must be developed and supported to include within their research goals the pursuit of prospective, controlled clinical trials of dietary supplements in children.
5. Health-care institutions should adopt best-practices guidance

with respect to policies and procedures regarding the use of herbs and dietary supplements for hospitalized children, under more precise stipulations promulgated by oversight agencies such as the Joint Commission.

6. New research and public policy initiatives should be supported to expand poisoning prevention to include inadvertent exposure of infants and children to herbs and dietary supplements and exposure to toxic contaminants and adulterants in some ethnic remedies and dietary supplements. New scientific inquiry and public policy are also needed to address the specific use of herbs and dietary supplements for goals of weight loss and enhancement of sports performance, as well as their intentional abuse by adolescents.

This is a critical area within a myriad of children's health interests that has been neglected while the commercial marketing of herbs and dietary supplements intended for children has experienced explosive, exponential growth. It is time to get serious about remediating the gaps in this area of children's health care.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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Assessing the Safety and Comparative Effectiveness of Follow-On Biologics (Biosimilars) in the United States

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As Congress begins drafting legislation concerning the US Food and Drug Administration (FDA) regulation of biosimilars, it is critical to keep in mind that these agents may differ from their innovator compounds. Therefore, it is of the utmost importance to be able to differentiate among innovators and biosimilars in administrative data in order to facilitate the conduct of population-based safety and comparative effectiveness studies. This Commentary proposes methods that would allow these agents to be distinguished in such data.

The patents for several biologic products manufactured using recombinant DNA technology are nearing expiration. Forthcoming generic biologics (also known as follow-on biologics or biosimilars) will be manufactured using biotechnology or derived from natural sources with the intent of being highly similar to one or more already-approved innovator products. This has led Congress to begin work on legislation under which the Food and Drug Administration (FDA) could approve follow-on biologics via an expedited approval process that would rely in part on scientific knowledge about the innovator product's safety and efficacy.[1] The rationale for encouraging the development of follow-on biologics is the same as that for encouraging generic small-molecule drugs: to reduce costs by fostering price competition. Indeed, availability of biosimilars is expected to result in savings of $9–12 billion to the US Medicare program over the next decade.[2]

Because several factors, including the larger size and higher degree of molecular complexity of biologic products compared with small-molecule drugs, the regulatory model of approving essentially exact copies of the same drug generally may not apply to biologics. In particular, the potential exists for real differences in the active molecules and therefore in the safety and effectiveness of different versions of the same biologic. This potential is not merely hypothetical. For example, changes to the manufacturing process of one version of epoetin alfa were associated with an increased risk of the hematologic abnormality known as pure red cell aplasia.[3] Other differences in safety or effectiveness could well emerge as use of biosimilars becomes widespread. However, it will be possible to identify such differences only if data are retained to distinguish among multiple versions of a given biologic. Complicating the ability to make this distinction is the fact that, as of this writing, it remains to be decided whether follow-on products will share the same nonproprietary (i.e., generic) name as the innovator product.

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